

1 IMPROVED FORMULATION FOR PROVIDING AN ENTERIC COATING
2 MATERIAL

3

4 The present invention relates to a formulation for
5 providing an enteric coating material and in particular
6 relates to such a material made up of food use approved
7 materials.

8

9 In many cases it is a requirement of pharmaceutical and
10 neutraceutical dosage units that they are able to pass
11 through the stomach intact and only release their
12 contents further down the GI Tract. This is necessary
13 when a particular ingredient (or ingredients) of the
14 dosage unit is unstable in the strongly acidic
15 environment of the stomach and where the ingredient or
16 ingredients are intended for release in the slightly
17 alkaline conditions of the GI Tract beyond the stomach.

18

19 The prior art shows many cases where pharmaceutical
20 dosage units achieve the abovementioned requirement using
21 an enteric coating. Enteric coating materials are
22 material types that are acid resistant, protecting and
23 preventing the dosage unit from a releasing of the

1 contents into the stomach. However, these coatings
2 dissolve or disintegrate in the neutral or mildly
3 alkaline conditions that are encountered beyond the
4 stomach. In the pharmaceutical industry enteric coatings
5 are widely used, with a wide choice of enteric materials
6 such as hydroxypropyl methylcellulose phthalate (HPMCP),
7 methacrylic acid/methyl methacrylate copolymers (for
8 example Eudragit™ materials), cellulose acetate phthalate
9 (cap) and polyvinyl acetate phthalate (PVAP). All of
10 these enteric materials have been developed over a
11 considerable period to provide a wide range of organic
12 solvent soluble materials or aqueous dispersions that
13 have both excellent coating and enteric properties.
14 However, manufacturers have had to invest heavily to gain
15 approval for the use of their materials in the
16 pharmaceutical industry and rigorous testing of the
17 materials has been required. Although all of these
18 products have been through this pharmaceutical approval
19 route, they have not been considered as viable
20 propositions for companies to devote similar significant
21 resources to gain approval for use in the food industry.
22 Therefore, although these materials are appropriate
23 enteric materials they are not approved for food use and
24 cannot legally be used to provide enteric coatings for
25 non-pharmaceutical dosage units. There are many cases
26 when it would be useful to provide enteric coatings on
27 items that are non-pharmaceutical dosage units, for
28 example for certain health foods etc.
29
30 There are in fact very few materials that are both
31 approved for food use and can be used as enteric
32 coatings. An example of a material that is approved for
33 food use and has been used or suggested as a enteric

1 coating material is Zein. Zein is a prolamine obtained
2 from corn and is used as a tablet binder or tablet
3 coating agent. It has in the past been used as an
4 enteric coating material and is insoluble in water and
5 most of the common organic solvents including both
6 acetone and ethanol. It can be dissolved and sprayed as
7 a film from propylene glycol/water solutions but due to
8 the high propylene glycol content (typically over 75%)
9 and high boiling point of propylene glycol, its use
10 suffers from technical, solution cost and environmental
11 consideration problems. Zein coats form a very weak film
12 in acid which, in tests, fail to resist 0.1 N HCl for two
13 hours. The coating does not dissolve in neutral or
14 mildly alkaline conditions and therefore does not perform
15 as a satisfactory enteric coating material. It again has
16 been suggested that the Zein coat is digested rather than
17 dissolved in the intestine, which is a rather unusual,
18 and non-enteric, release mechanism. Therefore Zein is
19 not particularly useful as an enteric non-pharmaceutical
20 coating.

21

22 Another possible material that has been suggested is
23 Shellac. Shellac is an exudate of the lac insect and is
24 a natural material that is insoluble in water but soluble
25 in organic solvents including ethanol. The term shellac
26 covers the range of this type of material. It has been
27 used as a sealing coat on tablet cores, as a food glaze
28 and also as a type on enteric coating. As Shellac is
29 insoluble in acidic conditions but soluble at higher pH
30 levels it would appear to be suitable as an enteric
31 coating material. However, reference texts describe
32 that, in practice, delayed disintegration and delayed
33 drug release occurs *in vivo* as the Shellac coat is not

1 soluble in the upper intestine. Laboratory trials in
2 this case have now shown that Shellac does not behave in
3 a typical enteric coating manner and instead behaves more
4 like an erodable coating, dissolving as a function of
5 time rather than of pH.

6

7 Traditionally, Shellac coats have been sprayed from an
8 organic solution, a disadvantage in terms of solution
9 cost and environmental protection cost. It is possible
10 to spray Shellac from an aqueous solution after forming
11 the Shellac into a water soluble alkali salt, and aqueous
12 Shellac salt solutions are commercially available. These
13 commercially available solutions form films that dissolve
14 in neutral or mildly alkaline conditions and appear, at
15 first consideration, to overcome the alkaline
16 insolubility problem of Shellac sprayed from organic
17 solution. However, unfortunately these films react
18 rapidly in acid to revert to the free acid Shellac and,
19 when ingested as a film of a dosage unit, the acidic
20 conditions in the stomach restore the film to Shellac and
21 restore the insolubility problem. Shellac films sprayed
22 as Shellac or as Shellac salts perform similarly and
23 neither resists acid (0.1 H NCl for two hours) and
24 rapidly (within one hour) releases the contents of the
25 dosage unit in neutral or mildly alkaline conditions in
26 the manner of an enteric coat. Shellac films can be
27 produced that disintegrate between two and three hours
28 and would appear to meet the above requirements. However
29 Shellac films are relatively insensitive to pH and, as
30 described above, disintegrate between two and three hours
31 regardless of the solution acidity or alkalinity and
32 instead behave as erodable films which dissolve as a
33 function of time.

1

2 It can be seen that it would be beneficial to provide an
3 enteric coating material that overcomes the problems of
4 the prior art.

5

6 It is an object of the present invention to provide an
7 enteric coating material.

8

9 According to a first aspect of the present invention
10 there is provided an enteric coating formulation
11 comprising shellac and alginate.

12

13 Preferably the alginate is sodium alginate.

14

15 Preferably the Shellac is in aqueous form.

16

17 Most preferably, the Shellac is in aqueous salt form.

18

19 Preferably the formulation is edible.

20

21 Most preferably the formulation comprises materials that
22 are approved for food use.

23

24 Optionally, the formulation comprises between 10-90%
25 Shellac.

26

27 Optionally, the formulation comprises between 10-90%
28 alginate.

29

30 Preferably, the formulation comprises equal quantities of
31 Shellac and alginate.

32

1 Preferably, the formulation is in the form of a spray
2 solution or a suspension.

3

4 Preferably, a low viscosity grade of alginate is used.

5

6 Preferably, the alginate has a viscosity of between 200
7 and 300 cps.

8

9 Optionally, a plasticiser may be added to the
10 formulation.

11

12 According to a second aspect of the present invention
13 there is provided a method of applying an enteric coating
14 formulation of the type described in the first aspect
15 wherein the formulation is applied to a dosage unit as a
16 spray.

17

18 Optionally, the pH of the formulation may be adjusted to
19 maintain a useable solution / suspension.

20

21 Optionally, the pH of any of the components of the
22 formulation may be adjusted to maintain a useable
23 solution / suspension.

24

25 According to a third aspect of the present invention
26 there is provided a dosage unit comprising enteric outer
27 coating which is itself comprises Shellac and alginate.

28

29 Preferably the alginate is sodium alginate.

30

31 According to a fourth aspect of the present invention
32 there is provided a method for preparing an enteric
33 coating comprising the steps mixing an aqueous solution

1 of an alkali salt of Shellac with an aqueous solution of
2 sodium alginate.

3

4 In order to provide a better understanding of the present
5 invention the invention will be described by way of
6 example only and with reference to the following drawing
7 in which Figure 1 shows a cross section of a dosage unit
8 comprising an enteric coating according to the present
9 invention.

10

11 Sodium alginate is GRAS listed and recognised as a food
12 additive in Europe. It is used as a stabilising agent,
13 suspending agent, tablet and capsule disintegrant, tablet
14 binder and viscosity increasing agent. However, until now
15 it has never been suggested as a constituent of an
16 enteric coating material. It is described in the art as
17 being insoluble below pH3 and slowly soluble in neutral
18 or alkaline solution and forms aqueous solutions.
19 Therefore it would not appear obvious to use sodium
20 alginate as part of an enteric coating.

21

22 Neither Shellac, in free acid or alkaline salt form, nor
23 sodium alginate form films that are acid resistant (where
24 an acid is 0.1 N HCl) and dissolve or disintegrate in
25 neutral/mildly alkaline conditions (i.e. pH 6.8 buffer),
26 i.e. neither performs the function of an enteric coat.

27

28 In the preferred embodiment of the present invention,
29 Shellac, in the aqueous salt form, and sodium alginate
30 are be mixed together to provide a formulation which
31 forms a film that resists acid but disintegrates in
32 neutral/mildly alkaline conditions. This film has the
33 properties of an enteric film and is entirely composed of

1 food use acceptable materials. Therefore, it is usable
2 by the food and nutraceutical industry to coat non-
3 pharmaceutical (i.e. non-licensed) dosage units where an
4 enteric coating may still be of great use.

5

6 In alternative embodiments, alginic acid, other salts of
7 alginic acid (alginates) or alginic acid derivatives such
8 as potassium alginate could be used in place of sodium
9 alginate.

10

11 As a preliminary step Shellac may be formed into a
12 solution of the alkali salt using standard techniques
13 known in the art. An example of such a technique is to
14 heat Shellac in water, with stirring, to 50-55°C then,
15 after dissolution of the Shellac and the addition of 10%
16 solution of ammonium hydrogen carbonate, the mixture is
17 heated to 60°C, with stirring for a further 30 minutes.
18 On cooling, the Shellac remains in solution as the alkali
19 salt.

20

21 The coating formulation is formed by mixing an aqueous
22 solution and of an alkali salt of Shellac with an aqueous
23 solution of sodium alginate. The content of either
24 material may vary from 10% of one to 90% and will still
25 demonstrate enteric properties in the film formed. Most
26 preferably the constituents are present in equal
27 quantities. The pH of the mixture, or either component
28 within the mixture, may be adjusted and selected to
29 maintain a useable solution or suspension.

30

31 The aqueous solution of the alkali Shellac salt may be
32 formed from Shellac as part of the preliminary process
33 using methods known in the art.

1
2 It is also worth noting that sodium alginate is
3 commercially available as different grades which form
4 solutions of wildly different viscosities. Preferably,
5 in this case, a low viscosity grade of sodium alginate
6 will be used. The preferred viscosity of the sodium
7 alginate is 200-300cps (centipoise), defined as a
8 viscosity of a 3% solution in water with a sequestering
9 agent.

10
11 A plasticiser may be added to the formulation to modify
12 the flexibility of the film formed to suit the dosage
13 requirements. Examples of plasticisers are
14 triethylcitrate, polyethylene glycol, polypropylene
15 glycol and glycerin monostearate. The plasticisers would
16 typically be added in the 5-25% range. The aqueous
17 Shellac/sodium alginate solution or suspension can, at
18 suitable concentration which is spraying system
19 dependent, be sprayed using commercial equipment by
20 personnel skilled in the art to form films on dosage
21 units.

22
23 It can be seen that the present invention has a number of
24 benefits over the prior art and up until now this
25 combination of materials has not been known to produce a
26 film that has enteric properties and is acceptable for
27 food use. As none of the materials themselves perform in
28 an enteric manner it is somewhat surprising to find that
29 the combination of material produces a film that shows
30 enteric properties, a property possessed by neither of
31 the components.

32

1 It should be noted that the embodiments disclosed above
2 are merely exemplary of the invention which may be
3 embodied in many different forms. Therefore, details
4 disclosed herein are not to be interpreted as limiting
5 but merely as a basis for claims and for teaching one
6 skills in the art as to the various uses of the present
7 invention in any appropriate manner.